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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/655,847	09/05/2003	William Gaarde	ISPH-0766	7081

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EXAMINER	
BOWMAN, AMY HUDSON	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/655,847	GAARDE ET AL.	
	Examiner	Art Unit	
	Amy H Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The restriction requirement mailed on 11/12/2004 has been withdrawn due to the amendment received on 3/16/2004, amending the claims to read on SEQ ID NO:18. The amended claims do not require restriction. If applicant is to amend the claims to include specific sequences in the future, a restriction may be set forth

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 9 broadly reads on any compound 8 to 80 nucleobases in length which specifically hybridizes with at least an 8-nucleobase portion of a preferred target region on any nucleic acid molecule encoding any PPAR-delta from any organism. The specification as filed does not describe a sufficient number of compounds to describe the structure and sequence of a sufficient number of species encompassed in the instantly claimed genus. The specification only teaches antisense sequences which

target PPAR-delta (table 1) that do not meet the scope of the instant claims. Although the specification describes antisense sequences (table 1) targeted to the human or mouse cells, there is no specific description provided of a compound to any other version or species of PPAR-delta which will specifically hybridize to any other PPAR-delta sequence, and inhibit the expression of any other PPAR-delta. The skilled artisan would not be able to envisage a sufficient number of antisense oligonucleotides targeted to other species of PPAR-delta such that the skilled artisan would recognize that the applicant was in possession of the claimed genus at the time of filing.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

MPEP 2163 states in part, "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004)

Thus, the instantly claimed invention cannot be said to have been adequately described in a way that would convey with reasonable clarity to those skilled in the art that, as of the filling date sought, applicant was in possession of the claimed invention

because the specification, while providing information on antisense sequences, does not provide a description of other species or guidance as to what antisense sequence for which version of PPAR-delta will target and inhibit a sufficient number of species of the gene in what species to describe the full genus claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Gray et al. (U.S. 5,856,103). Claim 1 is drawn to an antisense oligonucleotide 8 to 80 nucleobases in length wherein said antisense oligonucleotide specifically hybridizes to nucleobases 2056-2105 of a nucleic acid molecule encoding human PPAR-delta (SEQ ID NO:18). Instant claim 9 reads on any compound 8 to 80 nucleobases in length which specifically hybridizes with at least an 8-nucleobase portion of a preferred target region on a nucleic acid molecule encoding PPAR-delta. A preferred target region is defined in the specification, page 10, as being a region of the target nucleic acid that is accessible for hybridization, wherein the region is at least an 8-nucleobase portion of a target region to which an active antisense compound is targeted. As defined in the specification, pages 9 and 10, a sufficient degree of complementarity is the criteria for

specific hybridization. Gray et al. teach a 10 nucleotide antisense oligonucleotide with 90% complementarity to nucleobases 2056-2105 of SEQ ID NO:18 (see SEQ ID NO:3). Although Gray et al. do not specify that the 10 nucleotide antisense oligonucleotide be used to target a nucleic acid molecule encoding PPAR-delta, a different use does not materially change the composition. Therefore, the antisense sequence taught by Gray et al. meets the structural limitations of instant claims 1 and 9.

Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by McKay et al. (U.S. 6,159,734). McKay et al. teach two 20 nucleotide compounds with 100% complementarity to the target sequence instantly claimed (see SEQ ID NOS: 28 and 35). Although McKay et al. do not specify that the 20 nucleotide antisense oligonucleotides be used to target a nucleic acid molecule encoding PPAR-delta, a different use does not materially change the composition. Therefore, the antisense sequences taught by McKay et al. meet the limitations of instant claim 9.

Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Palmer et al. (WO 01/07066). Palmer et al. teach the use of antisense to the entire human PPAR-delta coding sequence, including portions of the untranslated regions, to inhibit foam cell formation from macrophages (see page 5, lines 17-31). Palmer et al. further teach that small size antisense compounds can be used to inhibit human PPAR-delta expression (see page 5, lines 19-21). Therefore, the teachings of Palmer et al. meet the limitations of claim 9.

Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Grimm et al. (U.S. 5,837,542). Grimm et al. teach a ribozyme comprising 15 nucleotide hybridizing

arms which are 100% complementary to SEQ ID NO:18, nucleobases 2056-2105 (See SEQ ID NO:553). As defined in the specification, antisense compounds include ribozymes (see page 14, lines 18-22). Although Grimm et al. do not specify that the 15 nucleotide antisense oligonucleotide be used to target a nucleic acid molecule encoding PPAR-delta, a different use does not materially change the composition. Therefore, the ribozyme taught by Grimm et al. meets the structural limitations of instant claim 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al. in view of Baracchini et al. (U.S. 5,801,154), further in view of Fritz et al.

Claims 2-8 specify that the antisense oligonucleotide of claim 1: comprise at least one modified internucleoside linkage, wherein the modified internucleoside linkage is a phosphorothioate linkage: comprise at least one modified sugar moiety, wherein the sugar moiety is a 2'-O-methoxyethyl sugar moiety; comprise at least one modified nucleobase, wherein the modified nucleobase is a 5-methylcytosine; or wherein the antisense oligonucleotide is a chimeric oligonucleotide. Claim 10 is drawn to a

composition comprising the antisense oligonucleotide of claim 1 and a pharmaceutically acceptable carrier or diluent. Claim 11 specifies the composition to further comprise a colloidal dispersion system.

Gray et al. teach a 10 nucleotide antisense oligonucleotide with 90% complementarity to nucleobases 2056-2105 of SEQ ID NO:18 (see SEQ ID NO:3) which meets the structural limitations of instant claims 1 and 9. Additionally, Gray et al. teach that modifications to the three portions of the nucleotide unit are beneficial to increase stability in the presence of nucleases (see columns 7 and 8). Gray et al. specifically discuss the value of using a phosphorothioate to inhibit nucleases. Gray et al. do not teach the modifications of claims 2-8 specifically to this oligonucleotide or the pharmaceutical compositions of claims 10 and 11.

Baracchini et al. teach antisense oligonucleotides formulated in a pharmaceutical composition (column 4). Baracchini et al. teach the modification of antisense oligonucleotides, such as phosphorothioates, 2'-O-methoxyethyl sugar moieties, and 5-methylcytosine nucleobase modifications (columns 6 and 7). Additionally, Baracchini et al. teach the usage of chimeric oligonucleotides containing two or more chemically distinct regions (column 8).

Fritz et al. teach a composition comprising an antisense oligonucleotide and a pharmaceutically acceptable carrier or diluent comprising a colloidal dispersion system.

Gray et al. teach an antisense sequence that meets the structural limitations of the instantly claimed antisense oligonucleotide. Although Grimm et al. do not teach the modifications of claims 2-8 or the pharmaceutical carrier of claims 10 and 11, it would

have been obvious to a person of ordinary skill in the art at the time the invention was made to use the sequence of Gray et al. in combination with the phosphorothioate, 2'O-methoxyethyl, 5-methylcytosine, or chimeric modifications taught by Baracchini et al. with the motivation to gain the known benefits of these modifications, which include enhanced cellular uptake, enhanced affinity for the nucleic acid target, and increased stability in the presence of nucleases (columns 6 and 8). Since Baracchini et al. specifically discuss the ability to deliver antisense oligonucleotides with these modifications and comprising a pharmaceutically acceptable carrier, there would have been a reasonable expectation of success to apply these modifications and conditions to the antisense oligonucleotide being instantly claimed. One of ordinary skill in the art at the time the invention was made would conclude that these modifications are applicable to the instant antisense oligonucleotide and that the modifications would enhance the effectiveness of the antisense oligonucleotides. Additionally, It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize a colloidal dispersion system, as taught by Fritz et al., with the motivation of gaining stability with low toxic side effects (see page 287, last paragraph). Therefore, the inventions of claims 1-11 would have been obvious, as a whole, at the time the instant invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is 571-272-0755. The examiner can normally be reached on Mon-Fri 7:30 am – 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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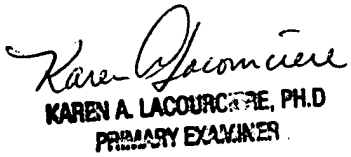

Amy H. Bowman
Examiner
Art Unit 1635